

Docket No. 3658-0103P

REMARKS

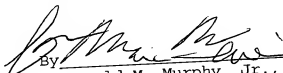
The specification has been amended to provide a cross-reference to the previously filed International Application. The claims have been amended to delete improper multiple dependencies and to place the application into better form for examination. Entry of the present amendment and favorable action on the above-identified application are earnestly solicited.

Attached hereto is a marked-up copy of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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3658-0103P

Attachment: Version With Markings Showing Changes Made

(Rev. 01/22/01)

Docket No. 3658-0103P

VERSION WITH MARKINGS SHOWING CHANGES MADE

The claims have been amended as follows:

1. (Amended) [Use] A method of detecting destructive joint diseases which comprises detecting collagenase 3 as a prognostic clinical marker for the detection of destructive joint diseases.

2. (Amended) [Use] The method according to Claim 1, wherein collagenase 3 is [used] detected for prognosis of the progression of rheumatoid arthritis (RA).

3. (Amended) [Use] The method according to Claim 1 or 2, wherein the collagenase 3 mRNA expression is determined qualitatively and quantitatively.

4. (Amended) [Use] The method according to Claim 1 or 2, wherein the collagenase 3 antigen, both as a pro-enzyme and also in an activated form, is determined qualitatively and quantitatively.

5. (Amended) [Use] The method according to Claim 1 or 2, wherein the catalytic activity of the activated collagenase 3 is detected.

Docket No. 3658-0103P

6. (Amended) [Use] The method according to Claim 1 or 2, wherein the quantitative relationships between collagenase 3 and its specific or unspecific inhibitors[, as the case may be,] are determined by determination of free collagenase 3 protein and of the same bound in complexes with inhibitors and compared.

7. (Amended) [Use] The method according to [one of the Claims 1 to 6] Claim 1 or 2, wherein the detection is done in tissues and body fluids.

8. (Amended) [Use] The method according to Claim 1 or 2, wherein synovial membrane preparations, cartilage and bone preparations or preparations of the synovial membrane/cartilage interface, obtained in synovectomies, artificial joint replacement, inter alia operative interventions, and also in biopsies are used as tissue.

9. (Amended) [Use] The method of Claim 7, wherein synovial fluid or blood are used as body fluids.

10. (Amended) [Use] The method of Claim 1, wherein collagenase 3 is used for the detection of an increased genetic predisposition for rheumatoid arthritis (RA).

11. (Amended) [Use] The method of the increase of the clinical relevance of the meaningfulness according to [one of Claims 1 to 10] Claim 1 or 2, wherein not only collagenase 3, but

Docket No. 3658-0103P

also further markers such as HLA antigens for the detection of a more severe progression of RA or markers such as certain patterns of HLA antigens for the detection of an increased genetic predisposition are used.

12. (Amended) [Use] The method according to [one of the Claims 1 to 11] Claim 1 or 2, wherein not only collagenase 3, but also MT1-MMP and/or gelatinase A act as prognostic markers by determination of their mRNA or protein expression, their amount and localization or their catalytic activity in tissues or body fluids[, as the case may be].